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L1            1 US20040034096/PN

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L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:60452  HCAPLUS
DN   140:128156
ED   Entered STN:  26 Jan 2004
TI   Preparation of cinnamide derivatives useful as selective MAO-B inhibitors
IN   Jolidon, Synese; Rodriguez, Sarmiento Rosa Maria; Thomas, Andrew William;
     Wostl, Wolfgang; Wyler, Rene
PA   F. Hoffmann-La Roche AG, Switz.
SO   PCT Int. Appl., 28 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07C235-34
     ICS  C07C255-54; A61K031-165; A61K031-275; A61P025-28
CC   25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
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Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004007429	A1	20040122	WO 2003-EP7231	20030707
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004034096	A1	20040219	US 2003-613785	20030703 <--
PRAI	EP 2002-15583	A	20020715		

OS MARPAT 140:128156

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention refers to cinnamide derivs. of formula I [wherein: R1 = alkyl, halogen, halogenoalkyl, CN, alkoxy, halogenoalkoxy; R21, R22, R23, R24 = H or F; R3 = H, alkyl; A = -C(R4):C(R5)-, -C(R4)(R6)-C(R7)(R5)-, or -C.tplbond.C-; R4, R5, R6, R7 = H, alkyl; n = 1-3] useful for treatment and prevention of diseases mediated by MAO-B inhibitors. Compds. I are especially useful for the treatment of Alzheimer's disease and senile dementia. For instance, compound II (example 1, IC50 = 0.083 .mu.mol for human MAO-B; >10,000 for human MAO-A) was prepared via etherification of 4-iodophenol by 3-fluorobenzyl bromide, Sonogashira reaction of CH2:C(Me)CO2Me with obtained compound III, subsequent hydrolysis and amidation.

ST cinnamide prepn MAO monoamine oxidase inhibitor

IT Anti-Alzheimer's agents
Human
(preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT Mental disorder
(senile psychosis, treatment of; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT Alzheimer's disease
(treatment of; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 9001-66-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B, inhibitors, mediated diseases; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 649740-30-7P, 1-(3-Fluorobenzyloxy)-4-iodobenzene 649740-31-8P, 3-[4-(3-Fluorobenzyloxy)phenyl]-2-methylacrylic acid methyl ester 649740-32-9P, 3-[4-(3-Fluorobenzyloxy)phenyl]-2-methylacrylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of cinnamide derivs. useful as MAO-B inhibitors)

IT 649740-29-4P, 3-[4-(3-Fluorobenzyloxy)phenyl]-2-methylacrylamide 649740-33-0P, 3-[4-(3-Fluorobenzyloxy)phenyl]-2,N-dimethylacrylamide 649740-53-4P, 3-[4-(3-Fluorobenzyloxy)phenyl]but-2-enoic acid methylamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of cinnamide derivs. useful as MAO-B inhibitors)
IT 649740-34-1P, 3-[4-(3-Fluorobenzyloxy)phenyl]-2-methylpropionamide
649740-35-2P, 3-[4-(3-Fluorobenzyloxy)phenyl]-2,N-dimethylpropionamide
649740-36-3P, 3-[4-(3-Fluorobenzyloxy)phenyl]propynoic acid amide
649740-40-9P, 1-[4-(3-Fluorobenzyloxy)phenyl]propynoic acid methylamide
649740-41-0P, 3-[4-(3,4-Difluorobenzyloxy)phenyl]propionamide
649740-42-1P, 3-[4-(3-Fluorobenzyloxy)phenyl]-N-methylacrylamide
649740-45-4P, 3-[4-(3-Fluorobenzyloxy)phenyl]acrylamide 649740-46-5P,
N-Methyl-3-[4-(4-trifluoromethylbenzyloxy)phenyl]acrylamide
649740-47-6P, 3-[4-(3,4-Difluorobenzyloxy)phenyl]-N-methylacrylamide
649740-49-8P, 3-[4-(4-Fluorobenzyloxy)phenyl]-N-methylacrylamide
649740-50-1P, 3-[4-(3-Cyanobenzyloxy)phenyl]-N-methylacrylamide
649740-51-2P, N-Methyl-3-[4-(4-methylbenzyloxy)phenyl]acrylamide
649740-52-3P, 3-[4-(3-Methoxybenzyloxy)phenyl]-N-methylacrylamide
649740-55-6P, 3-[4-(3-Fluorobenzyloxy)phenyl]-N-methylbutyramide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cinnamide derivs. useful as MAO-B inhibitors)
IT 93291-55-5P, 1-[4-(3-Fluorobenzyloxy)phenyl]ethanone 94530-63-9P,
3-(4-Hydroxyphenyl)-N-methylacrylamide 175136-19-3P,
3-[4-(4-Fluorobenzyloxy)phenyl]acrylic acid 423752-10-7P,
3-[4-(3-Fluorobenzyloxy)phenyl]acrylic acid 649740-37-4P,
[[4-(3-Fluorobenzyloxy)phenyl]ethynyl]-trimethylsilane 649740-38-5P,
1-(3-Fluorobenzyloxy)-4-ethynylbenzene 649740-39-6P,
[4-(3-Fluorobenzyloxy)phenyl]propynoic acid 649740-43-2P,
3-[4-(3-Fluorobenzyloxy)phenyl]acrylic acid 3-fluorobenzyl ester
649740-44-3P, 3-[4-(3-Fluorobenzyloxy)phenyl]acryloyl chloride
649740-48-7P, 3-[4-(3,4-Difluorobenzyloxy)phenyl]acrylic acid
649740-54-5P, 3-[4-(3-Fluorobenzyloxy)phenyl]but-2-enoic acid methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cinnamide derivs. useful as MAO-B inhibitors)
IT 80-62-6, Methyl methacrylate 99-93-4, 4-Hydroxyacetophenone 104-81-4,
1-Bromomethyl-4-methylbenzene 402-49-3, 4-(Trifluoromethyl)benzyl bromide 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl bromide 540-38-5, 4-Iodophenol 874-98-6, 1-Bromomethyl-3-methoxybenzene 1066-54-2, Trimethylsilylacetylene 7400-08-0, p-Cumaric acid 23838-70-2, 3-(4-Hydroxyphenyl)propionamide 28188-41-2,
3-Bromomethylbenzonitrile 85118-01-0, 3,4-Difluorobenzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of cinnamide derivs. useful as MAO-B inhibitors)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bentue-Ferrer, D; CNS DRUGS 1996, V6(3), P217 HCAPLUS
(2) Fournier Innovation Synergie; WO 9011997 A 1990 HCAPLUS
(3) Rano, T; TETRAHEDRON LETTERS 1995, V36(22), P3789 HCAPLUS

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MOST RECENT DERWENT UPDATE: 200446 <200446/DW>
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>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMODATE THE NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION NUMBERS. SEE ALSO:
http://www.stn-international.de/archive/stnews/news0104.pdf <<<

=> d all l4

L4 ANSWER 1 OF 1 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-191103 [18] WPIX
DNC C2004-075334
TI New cinnamide derivatives are monoamine oxidase B inhibitors useful for treating e.g. Alzheimer's disease and senile dementia.
DC B05
IN JOLIDON, S; RODRIGUEZ SARMIENTO, R M; THOMAS, A W; WOSTL, W; WYLER, R
PA (JOLI-I) JOLIDON S; (SARM-I) RODRIGUEZ SARMIENTO R M; (THOM-I) THOMAS A W; (WOST-I) WOSTL W; (WYLE-I) WYLER R; (HOFF) HOFFMANN LA ROCHE & CO AG F
CYC 101
PI WO 2004007429 A1 20040122 (200418)* EN 28 C07C235-34
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2004034096 A1 20040219 (200418) A61K031-277 <--
ADT WO 2004007429 A1 WO 2003-EP7231 20030707; US 2004034096 A1 US 2003-613785 20030703
PRAI EP 2002-15583 20020715
IC ICM A61K031-277; C07C235-34
ICS A61K031-165; A61K031-275; A61P025-28; C07C255-54
AB WO2004007429 A UPAB: 20040316
NOVELTY - Cinnamide derivatives are new.
DETAILED DESCRIPTION - Cinnamide derivatives of formula (I) are new.
R1 = 1-3C alkyl, halo, halo-(1-6C)alkyl, cyano, 1-6C alkoxy or halo-(1-6C)alkoxy;
R21-R24 = H or F;
R3, R4 = H or 1-3C alkyl;
A = C(R4)=C(R5), C(R4)(R6)-C(R5)(R7) or C triple bond C;
R5-R7 = H or 1-6C alkyl, and
n = 1-3.
An INDEPENDENT CLAIM is also included for the preparation of (I).
ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Antidepressant; Tranquilizer; Neuroleptic; Eating-Disorders-Gen.; Anorectic; Antiaddictive; Antismoking; Antiinflammatory.
MECHANISM OF ACTION - Monoamine oxidase B inhibitor.
The monoamine oxidase B enzymatic activity of 3-(4-(3-

fluorobenzyloxy)-phenyl)-2,N-dimethyl-propionamide (Ia) was assayed in 96-well-plates using a spectrophotometric assay adapted from the method as described in Zhou and Panchuk-Voloshina (A One-Step Fluorometric Method for the Continuous Measurement of Monoamine Oxidase Activity, Analytical Biochemistry 253:169-174 (1997)). The IC50 value of (Ia) was 0.029 micro mol.

USE - Used for treatment and prevention of Alzheimer's disease and senile dementia (claimed), acute and chronic neurological disorder, cognitive disorder, memory deficit, dementia, minimal cognitive impairment, Parkinson's disease, psychiatric diseases (e.g. depression, anxiety, panic attack, social phobia, schizophrenia, eating and metabolic disorder (e.g. obesity)), withdrawal symptoms induced by abuse of alcohol, nicotine and other addictive drugs and other neuroinflammatory diseases.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B10-A15; B10-D03; B14-C03; B14-D05C; B14-E11; B14-E12; B14-J01; B14-M01

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